

Oral Communication

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IDENTIFICATION OF THE HOMININ SIGNATURE TUNING THE DEVELOPMENT OF MULTIPLE HUMAN BRAIN REGIONS

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Human brain development is the outcome of a complex evolutionary history in which changes in developmental programs generated the anatomical and functional organization characteristic of *Homo sapiens*. In addition to selection and demographic processes, admixture with Neanderthals and Denisovans introduced genetic variants that persist in present-day genomes and may have contributed to inter-individual variation in neurodevelopmental trajectories. Here, we investigated whether this archaic genomic legacy can be detected in the genetic architecture underlying the development and organization of specific human brain regions. Using a curated set of 34,572 archaic introgressed biallelic (AIB) variants, we tested associations with 3,143 image-derived phenotypes (IDPs) from the UK Biobank, encompassing brain structure, function, and connectivity. We identified two genome-wide significant associations: chr20, located within *STK4* (P = 1.26E-09) associated with gray matter volume of the right superior frontal gyrus (RSFG), and chr5, within *ATG10* (P = 9.77E-10) associated with left putamen (LPU) volume. Importantly, *STK4* and *ATG10* participate in cellular pathways involved in the regulation of cell survival, proliferation, autophagy, and tissue homeostasis - processes fundamental to the formation, maturation, and remodeling of neural tissues. Their association with variation in two anatomically and functionally distinct regions therefore provides a potential link between archaic genetic variation and developmental mechanisms contributing to present-day brain morphology. The RSFG undergoes prolonged maturation and supports executive control, attention, and higher-order cognition, whereas the putamen is a major component of developing cortico-striatal circuits involved in motor control, learning, habit formation, and language-related motor planning. Our results suggest that archaic introgression may have contributed to fine-tuning developmental pathways affecting cortical and subcortical brain organization. Rather than representing a passive genomic legacy, introgressed hominin variation may therefore remain embedded in the developmental architecture generating modern human neuroanatomical diversity. Integrating evolutionary genomics and neuroimaging provides a powerful framework for reconstructing how interactions among different hominin lineages contributed to the development and evolution of the modern human brain.